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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/021,753	10/30/2001	Ken Fujise	UTSH:251US	6306
7590	11/17/2005			
FULBRIGHT & JAWORSKI L.L.P. A REGISTERED LIMITED LIABILITY PARTNERSHIP SUITE 2400 600 CONGRESS AVENUE AUSTIN, TX 78701			EXAMINER ANGELL, JON E	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 11/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/021,753	FUJISE ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-89 is/are pending in the application.
- 4a) Of the above claim(s) 1-38 and 48-62 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 39-47 and 63-89 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 October 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/7/2005 has been entered.

This Action is in response to the communication filed on 7/7/2005. The amendment filed 7/7/2005 is acknowledged. The amendment has been entered. Claims 1-89 are currently pending in the application and are addressed herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claims 1-38, 48-62 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/1/2004.

Claims 39-47 and 63-89 are examined herein.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39-47 and 63-89 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection was set forth in the previous Office Action and is reiterated below, for convenience.

The Written Description Guidelines for examination of patent applications indicates, “the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus.” (See MPEP 2100-164)

In the instant case, the claims encompass methods for identifying modulators of “a Fortilin polypeptide” and encompass a Fortilin polypeptide that is “at least 70% identical or functionally equivalent to SEQ ID NO: 2 or that has at least 20 contiguous amino acids from SEQ ID NO: 2” (see claims 38 and 68). Therefore, the claims encompass variants of SEQ ID NO: 2 which are different from the sequence disclosed as SEQ ID NO: 2 but which have not been adequately described.

As such, the instant claims encompass methods wherein the methods utilize variants of SEQ ID NO: 2 (human Fortilin) wherein the variant polypeptides could be any variant of Fortilin, including variants that have the same function as Fortilin, as well as variants that have a

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different function or which or non-functional variants. The genus of Fortilin variants encompassed by the claims includes homologues of human Fortilin which are found in different species of organisms. As such, the claims are drawn to the use of a molecule wherein the molecule can be any member of a huge genus of Fortilin variants. The specification has only described one species of this vast genus—the wild-type Fortilin polypeptide disclosed as SEQ ID NO: 2. The specification does not disclose any other variants of Fortilin that maintain Fortilin activity, nor does the specification indicate which amino acids of Fortilin can be changed or deleted and result in a “biologically active” Fortilin variant. Furthermore, there is no structure function relationship described such that one of skill in the art would be able to clearly recognize any critical structural elements of Fortilin. Considering the huge number of possible variants encompassed by the claims and the limited guidance provided in the specification with respect to identifying the biologically active variants encompassed by the claims, it is the Examiner’s position that the specification has not adequately described a sufficient number of “representative species” encompassed by the claims, as required.

Additionally, the art recognizes that although structural similarity can serve to classify a protein as related to other known proteins, this classification is insufficient to establish a function or biological significance for the protein because ancient duplications and rearrangements of protein-coding segments have resulted in complex gene family relationships. Duplications can be tandem or dispersed and can involve entire coding regions or modules that correspond to folded protein domains. As a result, gene products may acquire new specificities, altered recognition properties, or modified functions. Extreme proliferation of some families within an organism, perhaps at the expense of other families, may correspond to functional innovations

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during evolution. See Henikoff et al. (Science 1997; previously cited). Accordingly, one skilled in the art would not accept mere homology as establishing a function of protein because gene products may acquire new specificities, altered recognition properties, or modified functions. Rather, homology complements experimental data accumulated for the homologous protein in understanding the homologous protein's biological role. Although, the presence of a protein module in a protein of interest adds potential insight into its function and guides experiments, insight into the biological function of a protein cannot be automated. However, homology can be used to guide further research. (See Henikoff, paragraph bridging pages 613-614, through page 614, paragraph bridging columns 1-2).

Furthermore, the art recognizes that a high degree of structural homology may not result in functional homology. Witkowski et al. (Biochemistry 1999; previously cited) teaches that one amino acid substitution transforms a β -ketoacyl synthase into a malonyl decarboxylase and completely eliminates β -ketoacyl synthase activity. Seffernick et al. (J. Bacteriol., 2001; previously cited) teaches that two naturally occurring *Pseudomonas* enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Therefore, the claimed genus of "Fortilin" polypeptides has the potential of encompassing polypeptides that have different functions.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at

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page 1116). For the reasons indicated herein, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of Fortilin polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, the claims encompass a genus of "Fortilin" polypeptides that includes variants of human Fortilin which are structurally (and possibly functionally) different from those explicitly described in the specification. The claimed genus encompasses all possible "Fortilin" polypeptide variants that are at least 70% identical to or functionally equivalent to SEQ ID NO: 2 or that have at least 20 contiguous amino acids from SEQ ID NO: 2 (a huge number of possibilities). However, the specification has not adequately described a sufficient number of species or the critical functional elements common to the members of the genus. Therefore, the written description requirement has not been met and the rejection is proper.

It is noted that the specification does provide description of the human Fortilin polypeptide that is SEQ ID NO: 2, and limiting the claims to the Fortilin polypeptide that is SEQ ID NO: 2 would obviate this rejection.

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Claims 68-83 and 85-88 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

MPEP §2163.06 notes:

If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).

MPEP §2163.02 teaches that:

Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application.

MPEP §2163.06 further notes:

When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure.

The instant claims are drawn to:

A method of identifying a modulator of a Fortilin polypeptide comprising:

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(a) contacting a candidate modulator with a recombinant cell expressing a Fortilin polypeptide that is at least 70% identical or functionally equivalent to SEQ ID NO: 2 or that has at least 20 contiguous amino acids from SEQ ID NO: 2;

(b) measuring the level of Fortilin activity or expression of the cell; and,

(c) comparing the level of Fortilin activity or expression of the cell to the level of Fortilin activity or expression of a cell not contacted with the candidate modulator,

wherein a difference between the level of Fortilin activity or expression indicates that the candidate modulator is a modulator of a Fortilin polypeptide.

It is noted that claim 68 was amended prior to the Office Action mailed on 3/3/2005 such that the claim now encompasses using a recombinant cell expressing the Fortilin polypeptide. It is noted that claim 68 is not limited to a recombinant cell that that has been transfected with a nucleic acid that encodes and expresses Fortilin. In fact, given the broadest reasonable interpretation, the claims encompasses using a cell that has been transformed with anything wherein the cell expresses an endogenous Fortilin polypeptide.

Applicants have indicated in the response filed 5/13/05 that support for the amendment can be found in Example 9, pages 159-160 of the specification (see page 17 of the response filed 11/26/04).

Looking to the specification it is noted that with respect to a method using a recombinant cell for identifying compounds that “modulate a Fortilin polypeptide”, Example 9, pages 159-160 discloses, under the title “Identification of inhibitors of p53 Fortilin Interaction”

“[A] stable transfection will be established in mammalian cells. These cells will have stably transfected plasmids: i) A plasmid to produce the GALA-DNA-BD (binding domain)-Fortilin; ii) A plasmid to produce the VPI6-DNA-AD (activating domain)-ps3;

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and iii) A reporter plasmid that contain beta-galactosidase reporter gene under the control of a GAL4-responsive element and the minimal promoter of the adenovirus Elb.

The transfected cells will be seeded on 96 well plates. Candidate compounds will be dissolved in PBS (pH=7.4), added to the media, and incubated before cells are assayed for β -galactosidase activity. The lower the activity of β -galactosidase, the higher the inhibitory effect of the candidate compound.”

Therefore, the Example 9 does not disclose a method of identifying a modulator of a Fortilin polypeptide using a recombinant cell wherein the cell expresses endogenous Fortilin polypeptide. Example 9 does disclose a method of identifying an inhibitor of p53-Fortilin interaction, using a cell transfected with specific plasmids. Therefore, Example 9 is not commensurate in scope with the instant claims and thus does not provide the proper support required for the instant claims.

The Examiner has thoroughly searched the specification for support for the instant claims. The following disclosure was found in the specification: Example 12, (p. 161), cell line cells (in vitro) were stably transfected with a plasmid to expresses HA-Fortilin and interaction of the HA-Fortilin with p53 was assayed. Examples 13 and 15 (p. 162 and 163) a cell line cell (in vitro) was stably transfected to express Fortilin and Apoptotic activity in the cells were assayed. Example 14 (p. 162-163) a cell line cell (in vitro) was stably transfected to express Fortilin and Caspase-3-like activity was assayed in the cells. Example 15 (p. 163-164) cell line cells (in vitro) were transfected with a plasmid that expressed antisense-Fortilin polynucleotide and a plasmid expressing a reporter gene to determine anti-apoptotic activity of Fortilin. Example 16 (p. 164) cells were stably transfected (in vitro) with a plasmid that expressed HA-Fortilin and localization of Fortilin was determined. Also, Examples 17-22 (pp. 164-168) all encompassed stably transfecting cells (in vitro) with a polynucleotide that expresses a Fortilin polypeptide. It is

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noted that Examples 12-22 do not disclose methods for identifying modulators of Fortilin activity.

The only Example found in the specification that specifically discloses a method of identifying compound that affects Fortilin activity is the disclosure in Example 9 which is specifically drawn to identifying inhibitors of p53-Fortilin interaction using a cell (in vitro) stably transfected with the 3 plasmids indicated and performing the specific assay to determine if the candidate inhibits p53-Fortilin interaction.

It is noted that the specification (specifically, Example 9) does have support for a method of identifying an inhibitor of p53-Fortilin interaction using an in vitro recombinant cell that has been stably transfected with i) a plasmid to produce the GALA-DNA-BD (binding domain)-Fortilin; ii) a plasmid to produce the VPI6-DNA-AD (activating domain)-ps3; and iii) a reporter plasmid that contain beta-galactosidase reporter gene under the control of a GAL4-responsive element and the minimal promoter of the adenovirus Elb wherein the candidate inhibitor is contacted with the recombinant cell and beta-galactosidase activity is assayed wherein the lower the activity of β -galactosidase (compared to a proper control cell), the higher the inhibitory effect of the candidate compound.

It is noted, however, that the specification does not appear to have support for a method of identifying a modulator of Fortilin activity using a transfected cell wherein the cell expresses endogenous Fortilin.

Since proper support for amended claim 68 cannot be identified in the specification, the instant rejection is appropriate. It is noted that claim 69 indicates that Fortilin polypeptide is exogenous with respect to the cell, thus claim 69 does not encompass a transfected cell wherein

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the cell expresses endogenous Fortilin. As such, claim 69 is not included in the instant rejection. Amending claim 68 to indicate that the cell has been transfected with an exogenous nucleic acid that expresses SEQ ID NO: 2 (human Fortilin) would obviate this rejection.

Response to Arguments

Applicant's arguments filed 7/7/2005 have been fully considered but they are not persuasive.

With respect to the rejection of claims under 35 USC 112, 1st paragraph (written description), Applicants argue that the Federal Circuit has stated that the test for the written description requirement is “whether the application relied upon ‘reasonably conveys to the artisan that the inventor had possession at the time of the later claimed subject matter.’” Furthermore, Applicants argue that while a structure/function relationship may be relied upon to satisfy the written description requirement, it is not absolutely required. Applicants assert the specification fully supports any polypeptide that is at least 70% identical or functionally equivalent to SEQ ID NO: 2 or that has at least 20 contiguous amino acids from SEQ ID NO: 2. Applicants assert that a person of ordinary skill in the art would understand that the specification has disclosed at least *thousands* of different species with respect to SEQ ID NO: 2, that even an individual who is minimally skilled in the art could identify many different species that satisfied the claims based simply on the disclosed sequence, and that based on the number of disclosed species the specification necessarily satisfies the written description requirement because it reasonably conveys to one of skill in the art that they had possession of the claimed subject matter (see paragraph bridging pages 14-15 of the paper filed 7/7/2005).

In response, it is acknowledged that the test for the written description requirement is whether the application reasonably conveys to the artisan that the inventor had possession at the time of the later claimed subject matter. It is also acknowledged that while a structure/function relationship may be relied upon to satisfy the written description requirement, it is not absolutely required. However, the Examiner disagrees with Applicants' assertion that the specification fully supports any polypeptide that is at least 70% identical or functionally equivalent to SEQ ID NO: 2 or that has at least 20 contiguous amino acids from SEQ ID NO: 2 and that a person of ordinary skill in the art would understand that the specification has disclosed at least *thousands* of different species with respect to SEQ ID NO: 2. It is respectfully pointed out that the specification has only specifically disclosed 7 polypeptides of the broad genus of Fortilin polypeptides encompassed by the claims: wild-type Fortilin (SEQ ID NO: 2), three deletion mutants of Fortilin ($F_{\Delta 5-172}$, $F_{\Delta 23-172}$, and $F_{\Delta 46-172}$; e.g., see Example 21 pages 166-168), as well as the rabbit, mouse and chicken Fortilin sequence homologs which are disclosed to be 98%, 95% and 90% identical to SEQ ID NO: 2 (e.g., see Figure 1A). It is noted that the homologs of Fortilin that are disclosed as 98%, 95% and 90% identical to SEQ ID NO: 2 are homologs based solely on sequence alignment. There is no evidence of record which indicates that the sequence homologs have the same function as SEQ ID NO: 2. Furthermore, the specification only discloses that the wild-type Fortilin polypeptide (SEQ ID NO: 2) and the Fortilin deletion mutant comprising a deletion of amino acids 1-4 ($F_{\Delta 5-172}$) are able to bind MCL1 and inhibit etoposide-induced apoptosis (e.g., see Figure 16 and the paragraph bridging pages 16-17 of the specification). Therefore, one of ordinary skill in the art would not understand that the specification has disclosed at least *thousands* of different species with respect to SEQ ID NO: 2,

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rather one of ordinary skill in the art would only recognize that the specification has disclosed only 7 specific polypeptides encompassed by the claims. Considering that the claims are drawn to any polypeptide that is at least 70% identical or functionally equivalent to SEQ ID NO: 2 or that has at least 20 contiguous amino acids from SEQ ID NO: 2, the claims encompass possibly *millions* of different polypeptides, including polypeptides that have different functions as well as non-functional mutants. Therefore, the specification has not disclosed a “representative number” of polypeptides encompassed by the claims. Applicants are reminded that adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it, the compound itself is required (See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016), and one cannot describe what one has not conceived (See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483).

Therefore, Applicant’s arguments are not persuasive.

It is noted that Applicants have not rebutted the rejection of claims under 35 USC 112, 1st paragraph (new matter) set forth in the Office Action mailed 3/3/2005. As such the rejection is maintained.

Conclusion

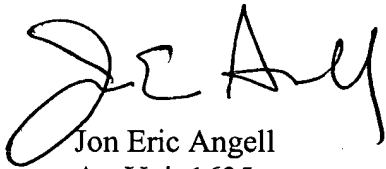
No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Jon Eric Angell
Art Unit 1635